REMARKS

I. Restriction Requirement

Claims 8, 9, and 12-18 remain pending. In the Office Action, the Office imposed a restriction requirement between claims 8, 9 and 12-15 (Group I) and newly added claims 16-18 (Group II). Office Action, page 2. According to the Office, claims 16-18 are "unrelated to the instant invention of group I, which is drawn to an RNA variant specifically adopting the secondary structure of SEQ ID NO: 4. The secondary structure of SEQ ID NO: 4 is not a limitation of the newly added claims." *Id.* at 3.

Restriction is proper only when two criteria are met. First, the inventions must be independent or distinct as claimed. Second, there must be a serious search burden on the Examiner. "If the search and examination of the entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions." M.P.E.P. § 803.

Here, the Office has not shown that these criteria are met. In particular, both of the allegedly separate and distinct inventions fall within class 435, subclass 6. The Office's search of the art relative to claims 8, 9 and 12-15 will also constitute a search of the subject matter of the claims 16-18. Further, although the Office asserts that each group is drawn to a different and distinct structure, the secondary structure of SEQ ID NO: 4 is the same as the secondary structure of tRNA, as recited in added claim 16. Claim 16 is simply a different way of describing the generic invention.

Because the subject matter of claims 8, 9 and 12-15 is drawn to the same genus as that recited in claims 16-18, there is no undue burden for the Offce to search all of

the pending claims. Applicants therefore respectfully request that the Office withdraw the restriction requirement.

II. Rejection Under 35 U.S.C. § 102(b)

The Office rejects claim 8 under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent No. 5,607,842 to Cohen et al. ("Cohen"). Office Action, page 4. In the rejection, the Office states that it is interpreting claim 8 as drawn to "an RNA variant adopting the secondary structure (I). *Id.* The Office points to Figure 4 of Cohen as the allegedly anticipatory structure.

To anticipate a claim under 35 U.S.C. § 102, every element recited in the claim must be disclosed in the reference. *See Verdegaal Bros. v. Union Oil Co. of California*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987) ("A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.") Further, a reference must "clearly and unequivocally disclose the claimed [composition] or direct those skilled in the art to the [composition] without any need for picking, choosing, and combining various disclosures . . . ." *In re Arkley*, 172 U.S.P.Q. 524, 526 (C.C.P.A. 1972).

Cohen's Figure 4 depicts a tRNA structure that lacks a bulge in the region that corresponds to the region in which hydrogen bonds form between nucleotides 8 to 14 and 73 to 79. Claim 8, in contrast, recites that the RNA variant "comprises a bulge structure introduced in the region in which hydrogen bonds form between nucleotides 8 to 14 and 73 to 79." Because the RNA shown in Figure 4 of Cohen does not include an introduced bulge, it does not disclose every element recited in claim 8. Cohen therefore

does not anticipate claim 8. Applicants respectfully submit that the rejection is thus in error and ask the Office to withdraw it.

III. Rejection Under 35 U.S.C. § 112, ¶2

Claims 8, 9, and 12-15 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Office Action, page 5. According to the Office, "[i]t is unclear whether the bulge is introduced into the secondary structure, or into the variant adopting the secondary structure." *Id.* The Office is also of the opinion that "if a bulge was introduced into the instantly depicted secondary structure (I), it is unclear which nucleotides would be considered nucleotides 8 to 14 and nucleotides 73 to 79 because a nucleotide bulge would shift the numbering of the nucleotides." *Id.* at 6. Finally, the Office states that it considers claim 9 indefinite because "[i]f all of the nucleotides in the region of 73 to 79 are substituted, then there would not be a duplex region to form a bulge as recited in claim 8." *Id.*

As Applicants noted in response to the previous Office Action, the claims encompass RNA variants comprising bulge structures of various sizes, introduced into RNA variants of various sequences. But breadth is not the same thing as indefiniteness. M.P.E.P § 2173.04, page 2100-215. Because claim 8 makes clear that the bulge structure is *introduced* in the region in which hydrogen bonds form between nucleotides 8 to 14 and nucleotides 73 to 79, it is clear that secondary structure (I) is a reference structure which is then modified as indicated. The claim language is as clear as the subject matter permits, which is all the law requires. *See* M.P.E.P. § 2173.02, page 2100-205; *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.,* 806 F.2d 1565, 1

U.S.P.Q.2d 1081 (Fed. Cir. 1986). Applicants therefore respectfully request the Office to withdraw the rejection.

IV. Rejection Under 35 U.S.C. § 112, ¶1

The Office also rejects claims 8, 9, and 12-15 under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. Office Action, page 7. The assertions are similar to the ones made under the second paragraph of Section 112 above. In particular, the Office finds that the specification does not describe "where nucleotides 8 to 14 or 73 to 79 would be located on [the RNA variant] that is neither described or disclosed, having the secondary structure of SEQ ID NO: 4." *Id.* Further, the Office asserts that Applicants are "claiming a genus wherein it is impossible to determine secondary or tertiary structure from an undisclosed primary sequence." *Id.* For support, the Office points to Jen et al., Stem Cells, Vo. 18, pp. 307-19 (2000) and argues that the reference indicates that RNA folding programs based upon free energy calculations often give unreliable depiction for in vivo relevance. *Id.* It is the Office's position that in order to support the claimed genus, a core sequence that a skilled artisan would recognize as a sequence that would adopt the secondary structure must be provided. *Id.* at 8. Finally, the Office asserts that the skilled artisan would not recognize what types of structures could be introduced as a "bulge" without losing the disclosed function of acting as means of transporting a ribozyme into the cytoplasm. *Id.*

"The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction

to practice . . . , reduction to drawings . . . , or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. . . ." M.P.E.P § 2163.II.A.3.a.ii, pages. 2100-174-75 (citing *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997) ("*Lilly*"). In *Lilly,* the court concluded that a claim to a genus of cDNAs encoding mammalian insulin was not adequately described by the disclosure of a single nucleotide sequence encoding rat insulin. *Lilly* at 1569. However, the court noted that adequate written description could be provided by "a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *Id.*

Unlike the situation in *Lilly*, Applicants describe several species falling within the scope of the genus. In particular, the Specification describes species Rz1, Rz2, and Rz3 in detail, and mentions ten additional species on page 37, lines 19-24. Thus Applicants submit they have described a representative number of species. Further, these RNA variants all share secondary structure (I). See Figure 1 and Specification page 37. As can be seen by comparing the structures in Figures 1A-1C with the reference structure shown in Figure 1E, secondary structure (I) is a substantial portion of the structure of the RNA variants. Applicants have also shown that only those structures that retain the overall secondary structure (I) function to transport an added RNA sequence from the nucleus to the cytoplasm. For example, Rz4, shown as Figure 1D, is not an RNA variant adopting secondary structure (I) and does not function to

transport the attached ribozyme into the cytoplasm. See the discussion of Rz4, Specification, pages 36-38. Under the Written Description Guidelines, this shared structure is also sufficient to show possession of the genus.

The Office's position that a core sequence must be provided also disregards the fact that the Written Description requirement can also be satisfied by the recitation of a structure. While structure in the biotechnology arts is often described by nucleic acid or amino acid sequence, this is not the only way to describe a structure. There is simply no reason to require a core sequence when a core structure is recited in the claims. As discussed above, SEQ ID NO: 4 in claim 8 describes a base structure that is modified by introducing a bulge structure in the region in which hydrogen bonds form between nucleotides 8 to 14 and nucleotides 73 to 79. The recitation of particular nucleotides in the claim identifies where within that reference structure the bulge is introduced, i.e., within the amino-acyl stem. In addition, Applicants provide examples in which different bulge structures are introduced.

Applicant's written description provides not only many working examples that constitute "a representative number of species," but the claims recite a shared structure that correlates with the transport of the RNA from the nucleus to the cytoplasm. Further, Applicants have shown that various bulge structures can be introduced. Applicants respectfully submit that the skilled artisan would have readily appreciated that Applicants were in possession of the claimed invention as a whole at the time the application was filed. The rejection should therefore be withdrawn.

Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Steven P. O'Connor

Dated: December 20, 2005

By: Reg. No. 41,225 For
Jean B. Fordis
Reg. No. 32,984